In the Office Action of April 5, 2001, claims 40-42, 45, 49-53, 56 and 59-60 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not sufficiently described in the specification so as to give one skilled in the art possession of the invention. This ground of rejection is respectfully traversed.

The Examiner states that the specification does not contain a written description of the invention, specifically with respect to the disclosure of chimeric constructs which would be operable in the invention.

In response, applicants point to page 9, lines 4 to 9, which specifically states that chimeric constructs between at least a portion of P-selectin or ligand and another inhibitory molecule are operable in the invention. This is clear verbal support for the term "chimeric constructs" as used in the claims. The expression "chimeric constructs" is intended to be broad, but broad expressions are clearly permissible and are not improper if enabled by the specification. Applicants have provided specific verbal support for the term "chimeric constructs", and this term is accordingly fully enabled by the specification.

Moreover, two (2) references have been cited in the specification in support of the disclosure of chimeric constructs. One of these references, Sako et al. *Cell,* 75(6), pages 1179-1186 (1993), provides specific enabling support for chimeric constructs. For example, page 1181 of Sako describes the preparation of a chimeric form of P-selectin fused to human Fc($LEC_{\gamma 1}$). See, in particular, page 1181, col. 1, line 6 to col. 2, line 2; and see also page 1184, bottom, under "Experimental Procedures". The present invention is not intended to be limited to this particular chimeric construct, however, and this is but one example of the type of chimeric constructs which can be used. A copy of the Sato et al. reference is attached for the Examiner's convenience.

The other reference, Mulligan et al., *Journal of Immunology,* 151, pages 6410-6417 (1993), also provides enabling support for chimeric constructs. In particular, note page 6411 of the reference which describes the preparation of P-selectin-Ig chimeras. The chimeric constructs of the Mulligan reference are described as being useful for repairing CVF lung injuries. A copy of the Mulligan reference is also included for the Examiner's convenience.

Claims 40-42, 45, 49-53. 56 and 59-60 have also been rejected under 35 U.S.C. 112, first paragraph, as lacking enablement in the specification. This ground of rejection is also traversed.

The Examiner states that the invention is not enabled for the use of chimeric constructs to treat or prevent atherosclerosis.

In response, applicants note that claim 40, in particular, and those claims dependent thereon, refer to atherosclerotic **lesions** and not atherosclerosis per se. As will be appreciated by those skilled in this art, atherosclerosis is a condition which results from the accumulation of such lesions or plaque over an extended period of time. Restenosis, on the other hand, is a condition which generally occurs after vessel-corrective surgery to open a blood vessel which has been occluded due to the long term effects of atherosclerosis. Restenosis results in the reoccurrence of a vessel blockage due, in part, to the presence of such lesions.

Moreover, applicants reiterate that Example 1 provides a clear indication that P-selectin is implicated in artheroschlerosis. From Example 1, one skilled in the art would reasonably conclude that inhibitors of P-selectin could be used to prevent or control the onset of atheroscleosis. Applicants note that claim 40 refers to "at least partially preventing ….the formation or growth of atherosclerotic lesions", and this is clearly demonstrated in Example 1. Further, P-selectin chimeric constructs are listed in the specification as the type of inhibitors which would be expected to have this effect. The Federal Circuit has rejected the notion that human clinical trials are necessary in order to provide enablement in a patent application claiming a drug or a treatment procedure. By providing an animal model and associated data, applicants are in full compliance with the standards for enablement as currently applied by the courts to medical and pharmaceutical inventions.

Claims 45 and 56 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. This ground of rejection is also traversed.

Claims 45 and 56 have now been amended to include the definition for the term "PSGL-1". This term is well known in the art as demonstrated, for instance, in the Sato et al. reference. See page 1180, lines 1-3 (col. 1) of the reference. Accordingly, claims 45 and 56 are now believed to be in full compliance with the provisions of 35 U.S.C. 112, second paragraph.

In view of the foregoing facts and reasons, this application is now believed to overcome the remaining rejections, and to otherwise be in proper condition for allowance. Accordingly, withdrawal of the rejections, and favorable action on this application is solicited. Entry of the foregoing amendment is appropriate at this time since it does not create any new issues, and serves to simplify the remaining issues in the application. The Examiner is invited to contact the undersigned at the telephone number listed below if this is believed to facilitate allowance of this application.

Respectfully submitted,

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DATE: June 5, 2001

MARKED-UP CLAIMS

40. (Three Times Amended) A method for at least partially preventing or reversing the formation or growth of atherosclerotic lesions in a mammal comprising:

providing a soluble chimeric construct comprising a P-selectin ligand or a fragment thereof and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with or after a vessel-corrective technique.

45. (Twice Amended) The method of claim 40, wherein said P-selectin ligand or a fragment thereof [chimeric construct] comprises [PSGL-1] P-selectin glycoprotein ligand-1 or a fragment thereof.

51. (Three Times Amended) A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing a soluble chimeric construct comprising a P-selectin ligand or a fragment thereof and another molecule, said chimeric construct being capable of inhibiting the interaction between P-selectin and a ligand of P-selectin; and

administering to a mammal an effective amount of said chimeric construct such that said P-selectin-ligand interaction is inhibited, wherein said chimeric construct is administered prior to, in conjunction with or after a vessel-corrective technique.

56. (Twice Amended) The method of claim 51, wherein said chimeric construct comprises [PSGL-1] P-selectin glycoprotein ligand-1 or a fragment thereof.